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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/257,188	02/25/1999	GREGORY M. GLENN	PM244954	1850

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EXAMINER

EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
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1644

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DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action SummaryApplication No.
09/257,188Applicant(s)
Glenn et al.Examiner
G.R. EwoldtArt Unit
1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/31/01, 7/8/02, 10/11/02, and 11.22.02.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25, 27-51, and 60-95 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25, 27-51, and 60-95 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>12</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendments and remarks, filed 12/31/01, 7/08/02, 10/11/02, and 11/22/02, are acknowledged.

2. Applicant's Terminal Disclaimer, filed 12/31/01, has been entered, obviating the double patenting rejections over copending U.S. Application No. 09/266,803. U.S. Application No. 09/316,069 has been abandoned, thus, obviating the double patenting rejections over said application.

3. In view of Applicant's amendments, Claims 8-20, 22, 38, 44, and 46-49 have been rejoined and all previous rejections have been withdrawn.

Claims 1-25, 27-51, and 60-95 are being acted upon.

4. The following are new grounds of rejection necessitated by Applicant's amendment.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-25, 27-51, and 60-95 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) The phrase, "but does not penetrate the skin's dermis," in Claims 1, 23, and 28, comprises a negative limitation not supported by the specification or claims as filed.

B) The term "potentiating" an immune response, and the phrase "such that said at least one antigen is processed by an antigen presenting cell and then presented to a lymphocyte to induce said immune response, and said at least one adjuvant potentiates said immune response," in Claims 23 and 28 is not supported by the specification or claims as filed. Note that the

scope of "potentiating" is significantly different that the scope of "inducing", which is disclosed in the specification.

C) The term "biological warfare agent" in Claim 36 is not disclosed in the specification or claims as filed.

D) The terms "live virus", and "virosome" in Claim 38 are not disclosed in the specification or claims as filed.

E) The term ADP-ribosylating exotoxin "derivative" in Claims 43 and 60-61 is not disclosed in the specification or claims as filed.

F) The phrase "formulation comprises a mutant ADP-ribosylating exotoxin" in Claim 48 is not disclosed in the specification or claims as filed.

G) The phrase "formulation comprises a mutant ADP-ribosylating exotoxin B subunit" in Claim 49 is not disclosed in the specification or claims as filed.

H) The phrase "formulation comprises a chemically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated" in Claim 62 is not disclosed in the specification or claims as filed.

I) The phrase "formulation comprises a genetic mutant of *E coli* heat-labile enterotoxin" in Claim 63 is not disclosed in the specification or claims as filed.

J) The phrase "formulation is comprised of antigen molecules as chemical or recombinant conjugates" in Claim 64 is not disclosed in the specification or claims as filed.

K) The phrase "formulation is comprised of at least some antigen molecules which lack adjuvant properties" in Claim 66 is not disclosed in the specification or claims as filed.

L) The phrase "wherein the antigen is biochemically purified" in Claims 75 is not disclosed in the specification or claims as filed.

M) The phrase "wherein the adjuvant is recombinantly produced" in Claims 76 is not disclosed in the specification or claims as filed.

N) The phrase "wherein the adjuvant is chemically synthesized" in Claim 77 is not disclosed in the specification or claims as filed.

O) The phrase "wherein the adjuvant is biochemically purified" in Claims 78 is not disclosed in the specification or claims as filed.

P) The limitations regarding the "separate antigen" and "separate adjuvant" formulations of Claims 87-95 are not disclosed in the specification or claims as filed.

Applicant's amendments, filed 12/31/01, 7/08/02, 10/11/02, and 11/22/02, indicate that no new matter has been added to the claims, however, no support for the specific new limitations set

forth above has been found in the specification or claims as filed.

7. Claim 85 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of inducing an antigen-specific immune response,
does not reasonably provide enablement for:

a method of inducing a mucosal immune response.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

As set forth in Ogra et al. (2001), "Little is known about the mechanisms underlying the induction of mucosal immunity ...", however, it is known that the induction of mucosal immunity is highly dependent upon the route of delivery of the immunization, possibly due to the fact that the mucosal immune system is highly compartmentalized. For example, the reference teaches that with cholera toxin, rectal immunization will achieve different results than will oral immunization, which will achieve different results than will intragastric immunization. It is noted that the specification discloses no data, no working examples, and no specific guidance regarding the induction of a mucosal immune response. Accordingly, the induction of said response must be considered to be highly unpredictable and thus, requiring of undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient any examples encompassing the limitation of the claimed invention, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 at 703-872-9306 (before final) and 703-872-9307 (after final).

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
February 18, 2003



Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600